Intramembrane proteases are membrane enzymes whose active site is buried below the surface of the biological lipid membrane, and which cleave other membrane proteins within their transmembrane domains. They are divided into four families according to their catalytic residues – aspartate, serine (often called rhomboids), metalloproteases and the recently described glutamate proteases. By proteolytic cleavage inside lipid bilayer they affect many significant biological processes such as metabolism of lipids, cell proliferation and adhesion, regulation of developmental signaling, degradation of signal peptides, and membrane protein quality control. This work focusses on the role of intramembrane proteases in various diseases and biological mechanisms associated with pathological processes. These are specifically Alzheimer’s disease, infection by unicellular parasites (Mycobacterium tuberculosis, Entamoeba histolytica and Plasmodium falciparum), maturation of hepatitis C virus, Bunyamwera virus and swine influenza virus, and mitochondrial dysfunction.